PACKAGE LEAFLET

SOBREPINA, 30 mg COATED TABLETS

SOBREPINA

Nimodipine

10/60 coated tablets dosed at 30 mg

COMPOSITION

Nimodipine ..... 30 mg

Excipient q.s.p. ..... 1 coated tablet

PHARMACEUTICAL FORM AND CONTENT IN NUMBER OF UNITS

Packs of 10 and 60 coated tablets dosed at 30 mg in Nimodipine.

DRUG THERAPEUTIC CATEGORY: Cardiovascular system. Vasodilators. Used as cerebral and/or peripheral vasodilators (IV.4.b).

NAME AND LOCATION OF THE PERSON RESPONSIBLE FOR MARKETING AUTHORIZATION

Baldacci Portugal, S.A.

Rua Cândido de Figueiredo, 84-B

1549-005 Lisbon

THERAPEUTIC INDICATIONS

Reduction of neurological deficit after subarachnoid hemorrhage.

CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients.

MOST FREQUENT OR SERIOUS SIDE EFFECTS

Nimodipine is generally well tolerated after oral administration. The most common side effect is a decrease in blood pressure, which may be dose-related and occasionally requires discontinuation of therapy.

Undesirable effects directly attributed to oral therapy with nimodipine in patients with subarachnoid haemorrhage are decreased blood pressure, edema and headache.

In general, the following undesirable effects may arise:

Cardiovascular effects

Common (~5%): blood pressure decrease in patients with subarachnoid haemorrhage, requiring discontinuation of therapy in approximately 1% of cases.

Uncommon (<1%): Dose-related dyspnoea and edema in patients with subarachnoid haemorrhage, electrocardiogram (ECG) abnormalities including tachycardia and bradycardia, palpitations, flushing, rebound vasospasm, and hypertension. With nimodipine doses of 90 mg 4 times a day, congestive heart failure, pulmonary edema and ventriculitis.

Haematological effects

Uncommon (<1%): Thrombocytopenia, anemia, disseminated intravascular coagulation, deep vein thrombosis, low platelet count and pulmonary embolism in patients with subarachnoid haemorrhage.

Dermatological effects

Uncommon (<1%): rash requiring discontinuation of therapy in at least one case, acne, pruritus, diaphoresis and hematoma.

Gastrointestinal effects

Uncommon (<1%): Lower abdominal discomfort or cramps and constipation in patients on long-term treatment. Diarrhea in patients with subarachnoid haemorrhage.

Rarely: Intestinal pseudo-obstruction and “ileus”, vomiting and gastrointestinal bleeding.

Liver effects

Uncommon (<1%): Elevation of one or more liver function outcomes, including elevated serum concentrations of LDH, alkaline phosphatase, or ALT (SGPT) in patients with subarachnoid haemorrhage. Reversible increase in creatine kinase (CK, creatine phosphokinase, CPK), AST (SGOT), ALT, γ-glutamyl-transferase (GGT, γ-glutamyl-transpaptidase, GGTP), bilirubin and amylase, mainly during IV administration of nimodipine .

Additionally, hepatitis and jaundice.

Nervous System effects

Uncommon (<1%): Mental depression, headache, dizziness, neurological deterioration and hydrocephalus.

Additionally, and in individual cases, confusion with psychosis and exacerbation of insomnia.

Other effects

Uncommon (<1%): Muscle pain or cramps, wheezing, and hyponatraemia.

Rarely: Elevated serum glucose concentration and/or hyperglycaemia.

Additionally, pneumonia and wound infection.

DRUG INTERACTIONS

SOBREPINA interactions with the following drugs may be verified:

- Calcium channel blockers

Some in vitro studies suggest that diltiazem potentiates the negative inotropic effect of Nimodipine, according to a reversible and stereospecific mechanism. Although the clinical value of this result has not been determined, it is preferable to avoid the therapeutic association of nimodipine with calcium channel blockers.

- hypotensive agents

Nimodipine has been reported to potentiate the effects of concurrently used antihypertensive drugs. As low blood pressure or hypotension occurs when patients take Nimodipine alone, in the case of combination therapy with an antihypertensive, patients should carefully monitor their blood pressure in order to detect any need to reduce dosing or interrupt the hypotensive drug, and/or starting pharmacological blood pressure support.

Short-acting hypotensive agents should preferably be used.

- Cimetidine

A case of increase in the area under the plasma concentration-time curve and in the mean maximum plasma concentrations of Nimodipine of, respectively, 90% and 50%, when it was administered concomitantly with cimetidine, was described. However, no clinically important changes have been described with this association.

- Anticonvulsant agents

One case of phenytoin toxicity was observed in a patient with subarachnoid hemorrhage receiving Nimodipine. However, the majority of patients with subarachnoid haemorrhage on concomitant treatment with Nimodipine and phenytoin or barbiturates did not show signs of drug interactions.

Therefore, it is recommended to monitor patients and plasma phenytoin concentrations whenever starting or stopping Nimodipine therapy in a patient taking phenytoin.

- Other drugs

Limited data suggest that Nimodipine does not interact with anesthetic agents during surgery, and does not alter the pharmacokinetics and hemodynamic effects of digoxin.

Some in vitro data suggest that Nimodipine may enhance the cytotoxic effects of some antineoplastic agents, although the clinical importance of these data has not been determined.

SPECIAL PRECAUTIONS FOR USE

Although the fall in blood pressure is not sharp with normal oral doses of nimodipine, regular monitoring of blood pressure and pulse should be carried out during treatment with SOBREPINA.

Patients with impaired liver function (eg, cirrhotic patients) may have substantially reduced clearance of nimodipine. Therefore, in these patients, in addition to reducing the SOPREPINA dosage, monitoring of blood pressure and heart rate should be carried out.

EFFECTS ON PREGNANT WOMEN, INFANTS, CHILDREN, THE ELDERLY AND PATIENTS WITH SPECIAL PATHOLOGIES

Pregnancy

Although there are no adequate and controlled studies in humans to date, animal studies do not recommend its use in pregnant women. Nimodipine should be used in pregnancy only when the potential benefits justifies the possible risks to the fetus.

Breastfeeding

Nimodipine and/or its metabolites are distributed in the milk of animals (rats) in concentrations much higher than those in maternal plasma. As it is not known whether the drug is distributed in human milk, breastfeeding is not recommended during administration of Nimodipine.

Children

The safety and efficacy of SOPREPINA has not yet been established in individuals under the age of 18 years and therefore it should not be used in this age group.

Seniors

In elderly patients, the dose to be administered should be selected with care, as these patients often experience reduced liver, renal and cardiac functions, as well as the concomitant use of other medications.

Special Pathologies

Patients with impaired liver function (eg, cirrhotic patients) may have substantially reduced clearance of nimodipine. Therefore, in these patients, in addition to reducing the SOPREPINA dosage, monitoring of blood pressure and heart rate should be carried out.

EFFECTS ON THE ABILITY TO DRIVE AND USE MACHINES

SOPREPINA does not affect the ability to drive and use machines.

EXCIPIENTS WHOSE KNOWLEDGE IS IMPORTANT FOR CONVENIENT USE OF THE MEDICINAL PRODUCT

SOPREPINA includes Lactose. Patients with rare problems of hereditary galactose intolerance, lactase insufficiency or glucose/galactose malabsorption syndrome, should not take this medicine.

USUAL DOSAGE

The usual dosage is 30 mg three times a day (1 tablet every 8 hours). This dose may be doubled (2 tablets every 8 hours) if an ischemic risk arises.

Liver failure

Patients with hepatic impairment (eg cirrhosis) may have substantially reduced clearance of nimodipine and peak plasma concentrations may be significantly higher than in patients with normal hepatic function.

Thus, the dosage of nimodipine should be reduced with monitoring of blood pressure and heart rate; if necessary, vasopressors (norepinephrine or dopamine) can be used to support blood pressure.

Renal insufficiency

A reduction in nimodipine clearance has also been reported in patients with renal impairment, although age-related hepatic impairment may have contributed to this reduction in clearance. Therefore, in these patients, careful monitoring should be carried out.

Other cases where it may be necessary to reduce the dosage

In patients with low body weight and in patients with unstable blood pressure it is recommended to start treatment with careful monitoring.

The duration of treatment is, as a rule, 3 weeks, but it can vary depending on the duration of the vasospasms.

METHOD AND ROUTE OF ADMINISTRATION

Oral use: SOBREPINA tablets must be swallowed with the help of water.

INDICATION OF THE MOST FAVORABLE TIME FOR SOBREPINA ADMINISTRATION

The tablets should be taken outside meals, and the interval between takings should not be less than 4 hours.

MEDIUM DURATION OF TREATMENT WITH SOBREPINA

The duration of treatment is, as a rule, 3 weeks but it can vary depending on the duration of the vasospasms.

ATTITUDE TO TAKE WHEN ONE OR MORE DOSES IS OMITTED

If you have missed a dose, take it as soon as you find it is missing. However, if it is almost time for your next dose, skip the missed dose and continue treatment at your regular schedule.

In case you have missed more doses, follow the procedure above.

INDICATION OF HOW TO SUSPEND THE TREATMENT

Not applicable.

MEASURES TO BE TAKEN IN CASE OF OVERDOSE AND/OR INTOXICATION

In general, Nimodipine overdose is expected to produce effects that are the extension of its pharmacological and secondary effects, mainly cardiovascular effects such as excessive peripheral vasodilation leading to high systemic hypotension.

Management of overdose with nimodipine generally involves symptomatic and supportive care, and active cardiovascular support such as administration of a vasopressor agent (eg, norepinephrine, dopamine) may be necessary if clinically important hypotension occurs.

Since Nimodipine extensively bounds to plasma proteins, peritoneal dialysis or hemodialysis does not appear to be beneficial in removing the drug.

WARNINGS

If you notice any undesired side effects not listed in this leaflet, please tell your doctor or pharmacist.

Check the expiration date written on the package. Do not use SOBREPINA after the indicated date.

PARTICULAR STORAGE PRECAUTIONS

Do not store above 25°C. Keep in the original packaging.

SPECIAL PRECAUTIONS FOR THE DESTRUCTION OF UNUSED PRODUCTS

Normal precautions should be taken in disposing of drug residues.

DATE ON WHICH THE LEAFLET WAS LAST REVISED: July/2008